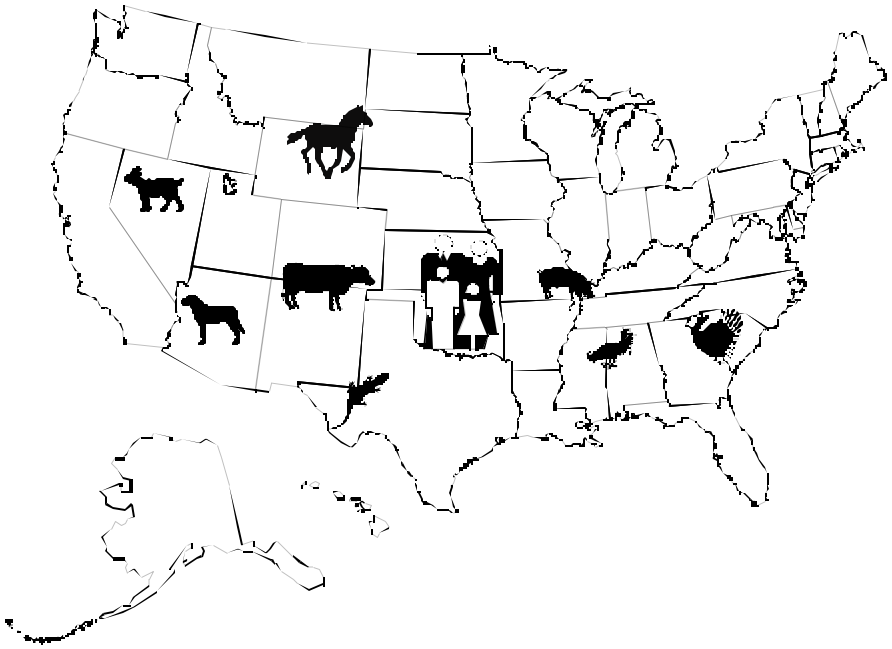
National Antimicrobial Resistance Monitoring System - Enteric Bacteria



A program to monitor antimicrobial resistance in humans and animals

Antibiotic resistance in foodborne pathogens is an increasingly important health issue. There is a program in place to monitor changes in susceptibility of enteric bacteria to antimicrobial drugs used in animals and humans. That program is the National Antimicrobial Resistance Monitoring System - Enteric Bacteria (NARMS).

FIRST, SOME BACKGROUND –

What is an antibiotic?

An antibiotic is an agent produced by organisms such as fungi and bacteria that kills or slows the growth of other microorganisms, particularly bacteria. An antibiotic is a type of antimicrobial drug. Antibiotics and other antimicrobial drugs enable doctors to cure bacterial illnesses like ear infections and strep throat in humans. Antibiotics and antimicrobial drugs are also used to treat or prevent illness in animals and in other areas of agriculture. There are also antimicrobial compounds found in many of the cleaning products marketed today. The use of all these antimicrobial compounds can lead to development of antimicrobial resistance in organisms exposed to them.

What is an antibiotic-resistant infection?

Resistant bacteria are not as susceptible to antibiotics as non-resistant bacteria. The use of antibiotics may eliminate susceptible bacteria, leaving resistant bacteria behind. If resistant bacteria spread, a person or animal with this infection may not be able to be treated with the usual antibiotics, or an increased dose may be required. As a result they may be sick for a longer time than if they had an infection caused by bacteria that were easily treatable with antibiotics.

How does resistance develop?

The increase in bacterial antimicrobial resistance is a natural phenomenon, an outcome of evolution. Any population of organisms, including bacteria, naturally includes variants with unusual traits. In this case, some bacteria have the ability to fend off the action of an antimicrobial. The use of antimicrobial drugs in humans and animals over the past 50 years has inadvertently accelerated the development of resistance by increasing the selection pressure exerted on these organisms. Once antimicrobial pressure has been introduced into an environment, resistance may be spread to other microbes.

Food animals such as cattle, pigs, turkeys, or chickens may receive antimicrobial drugs for growth promotion and control or treatment of infectious diseases. Food animals can carry organisms that can make people sick, but may not necessarily make the animal sick. For example, *Salmonella*, *Campylobacter* and *E. coli* O157 are common bacteria found in the intestines of various food animals. These bacteria may not cause disease in the animal, however, all three bacteria may cause foodborne illness in humans. These organisms may

develop resistance when exposed to antibiotics given to the animal. These resistant organisms can contaminate food products at slaughter and then infect humans who eat the food, particularly if the food is undercooked or cross-contaminated after cooking.

Evidence of increasing resistance to antimicrobial drug treatment in bacteria that infect humans has raised questions about the role that antimicrobial drug use in food animals plays in the emergence of antimicrobial drug resistant bacteria. The link between antimicrobial resistance in foodborne pathogenic bacteria and use of antimicrobials in food animals has been reported in a number of studies. For foodborne pathogens, especially those such as *Salmonella* that are rarely transferred from person to person in the United States, food (such as meat or eggs) from food animals is considered a likely source of most antimicrobial resistance.

How we monitor

We need to carefully watch for trends in levels of resistance to antibiotics. The United States now has a system in place that allows the Food and Drug Administration (FDA) to monitor resistance to antimicrobial drugs used in humans and food animals. The system is called the National Antimicrobial Resistance Monitoring System - Enteric Bacteria (NARMS). It combines the activities of FDA, the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA) to create a nationwide monitoring system. NARMS was started (and has been expanded) because of the human health concerns related to the use of antimicrobial drugs in food animals. As a part of NARMS, isolates of foodborne bacteria such as *E. coli*, *Salmonella*, Enterococci, and *Campylobacter* from humans and food animals are collected and tested to determine changes in bacterial susceptibility to antimicrobial drugs. Each year, samples are taken and tested to determine whether there have been changes over time in the resistance (or susceptibility) of certain enteric bacteria to a collection of antimicrobial drugs. The antimicrobial drugs tested are selected based on their importance in human and animal medicine. The food animal specimens are gathered from healthy farm animals, animal clinical specimens, from carcasses of food animals at slaughter, and from retail meats.

The human-origin isolates are sent in by 28 state and local departments of health: California (San Francisco, Contra Costa and Alameda counties), Colorado, Connecticut, Florida, Georgia, Hawaii, Kansas, Los Angeles County, Louisiana, Maine, Maryland, Michigan, Minnesota, Massachusetts, Montana, Nebraska, New Jersey, New Mexico, New York City, New York, Oregon, South Dakota, Tennessee, Washington, West Virginia, and Wisconsin, for testing conducted at the National Center for Infectious Disease, CDC, in Atlanta, Georgia. Sixty three percent (63%) of the United States population resides in states which submit human isolates to NARMS.

Animal-origin isolates are collected nationwide and submitted for susceptibility testing conducted by the Agricultural Research Service (ARS) of USDA in Athens, GA. Animal isolates are received from a number of sources including federally inspected slaughter and processing facilities, USDA National Animal Health Monitoring Studies on farms, and Veterinary Diagnostic Laboratories such as USDA's National Veterinary Services Laboratory. CDC and USDA test *Salmonella, E. coli, Campylobacter,* Entercocci, and other bacterial isolates for susceptibility to a panel of selected antimicrobial drugs. The results of these tests are compared with data from previous years to look for changes in resistance patterns of the organisms to these drugs.

NARMS reports are published annually.

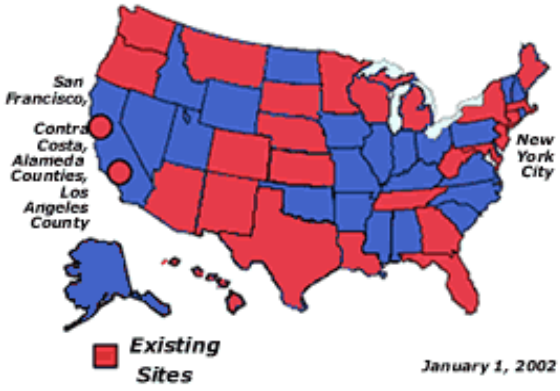
Where Can I Find NARMS Data?

NARMS data can be accessed through links on CVM home page:
(**www.fda.gov/cvm/index/narms/narms_pg.html**).

OR

Human data is located on the CDC web site:
(**www.cdc.gov/narms**).

Animal data may be directly accessed on the USDA web site:
(**www.arru.saa.ars.usda.gov/narms.html**)



Public health officials, animal producers, drug manufacturers, physicians, and veterinarians can use the information from NARMS to control and prevent harm from the use of antimicrobial drugs in food animals. The NARMS program was expanded in 2001 and 2002 to include testing of retail meats and animal feed ingredients. The FDA CVM Office of Research Laboratory in Laurel, MD is conducting susceptibility testing of these isolates.

NARMS Methods

Human arm: participating human public health departments forward every tenth *Salmonella* isolate, every tenth *Shigella* isolate and every fifth *E. coli O157:H7* isolate received at their public health laboratories to CDC for antimicrobial susceptibility testing. Nine of the NARMS health department partners, which also participate in the FoodNet Program, send *Campylobacter* isolates each week to the CDC Foodborne and Diarrheal Diseases Laboratory for susceptibility testing. States which submit Campylobacter isolates include California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee) *Listeria,* and *Vibrio* human isolates are also tested. The antimicrobial susceptibility testing results are sent from the CDC laboratory to NARMS epidemiologists at CDC, where data are entered and analyzed.

Collection sites for human isolates*

* effective January 2003, human data will be collected in all 50 states and three local health departments (District of Columbia, Los Angeles County and New York City).

Animal arm: The USDA, ARS, Antimicrobial Resistance Research Unit (ARRU) laboratory in Athens, Georgia receives *Salmonella*, *Campylobacter*, *E. coli* and Enterococci isolates from animals for antimicrobial susceptibility testing. Isolates are selected nationwide from research conducted by the USDA or collaborators, from National Animal Health Monitoring System studies conducted by USDA/Animal and Plant Health Inspection Service (APHIS), from diagnostic sources (such as National Veterinary Services Laboratories and sentinel sites which are veterinary diagnostic laboratories), and from raw product collected from federally inspected slaughter and processing establishments.

Animal isolates are collected nationwide

Three additional components have been added to the NARMS program that include sampling of animal materials. An **animal feed ingredient survey** collects samples of meat meal, meat and bone meal, fish meal, blood meal, and poultry meal collected at rendering plants in the U.S. These samples are tested for *Salmonella, E. coli, Campylobacter* and Enterococci. The **Iowa Retail Meat Pilot Survey** includes collection and antimicrobial susceptibility testing of bacterial isolates from retail meats purchased from Iowa retail grocery stores. A total of 870 samples of ground beef, ground turkey, pork chops, and chicken breasts were collected from 300 randomly selected sites. These samples are being cultured for *Salmonella, Campylobacter, E. coli*, and Enterococci. The collection phase of the Iowa Retail Meat Pilot Survey was completed in June, 2002. Susceptibility testing of isolates and data analysis is ongoing. A **FoodNet Retail Meat Surveillance** study began in January, 2002. Samples of ground beef, ground turkey, pork chops and chicken breasts are being collected in Connecticut, Georgia, Maryland, Minnesota, and Tennessee. Isolates from these samples are being sent from the state laboratories to FDA/CVM Office of Research for antimicrobial susceptibility testing of *Salmonella, Campylobacter, E. coli,* and Enterococci.

The NARMS program is designed with comparable methodology between the human and animal arms. For both human and animal isolates, susceptibility testing currently involves the determination of the minimum inhibition concentration (MIC) for a panel of selected antimicrobial agents. For *Salmonella* isolates, the antimicrobial drugs tested in 2002 include: amikacin, ampicillin, amoxicillin/clavulanic acid, ceftiofur, ceftriaxone, cephalothin, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfamethoxazole, tetracycline, trimethoprim/sulfamethoxazole and cefoxitin. These antimicrobial drugs are evaluated each year for their importance in human and animal medicine. The antimicrobial drugs tested can be modified to meet monitoring needs. Susceptibility testing of *Campylobacter* is performed to determine the MICs for eight antimicrobial agents: azithromycin, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, gentamicin, nalidixic acid and tetracycline. National Committee for Chemical Laboratory Standards (NCCLS) guidelines are followed, when available, throughout the testing procedure.

What Can NARMS Tell Us?

The NARMS program was begun in 1996 with Salmonella as the sentinel organism. Other enteric bacteria were added as the program was expanded. NARMS results for Salmonella are available since 1997. Links to the summary data are posted on the FDA CVM web site (see above). This data can provide useful information about patterns of emerging resistance, which in turn can help guide treatment decisions. NARMS data are an asset to outbreak investigations. Antimicrobial resistance patterns are useful in identifying the source and magnitude of resistance. Antimicrobial resistance data from humans and animals are important for the development of public health recommendations for the use of drugs in humans and food animals.

What Else is Being Done?

FDA's Center for Veterinary Medicine has developed a comprehensive approach to combat the complex problem of antimicrobial resistance. In January 1999, the Agency published a concept paper titled "Proposed Framework For Evaluating And Assuring The Human Safety Of The Microbial Effects Of Antimicrobial New Animal Drugs Intended For Use in Food-Producing Animals" (Framework Document). The Framework Document discussed possible strategies for managing the potential risks associated with the use of antimicrobial drugs in food- producing animals. The strategies included: 1) revision of pre-approval safety assessment for antimicrobial resistance for new animal drug applications to assess all uses; 2) categorization of antimicrobial drugs based upon the importance of the drug for human medicine; 3) post-approval monitoring for the development of antimicrobial drug resistance; 4) the collection of food animal drug use data; and also 5) the establishment of regulatory thresholds. FDA's goal is to protect the public health by ensuring that significant human antimicrobial therapies are not lost due to use of antimicrobials in food-producing animals, while providing for the safe use of antimicrobials in food-producing animals.

After holding several public meetings to obtain comments and feedback from various stakeholder groups, CVM expects to publish Guidance for Industry to implement the various strategies and concepts discussed in the Framework Document. In developing draft guidance,

CVM will consider all relevant comments recorded at the public meetings as well as relevant comments received in writing. In addition to the guidance document, additional guidance documents, as well as new or amended rules, may be necessary to fully implement the Framework Document concepts. Please refer to the FDA CVM web site for the latest information on publications to implement the Framework Document (**www.fda.gov/cvm**).

In addition to the work being done by CVM, veterinary and producer groups are developing prudent and judicious antimicrobial drug use programs to help veterinarians and producers make safe and sound decisions about the use of these products in animal production.

Using NARMS as a template, FDA CVM and Mexico are working together on a cooperative project known as ***"ResistVet"*** to conduct monitoring for trends in antimicrobial resistance in humans, animals, and retail foods at four sites in Mexico. To further support antimicrobial resistance monitoring in Mexico, FDA CVM collaborated with the World Health Organization to conduct a training course in 2001 on the surveillance of Salmonella and antimicrobial resistance in foodborne pathogens. The training took place at a participating ***ResistVet*** site in Mexico.

The ultimate goal of all of these programs is to make sure that antimicrobial drugs remain effective to treat human diseases. Information from NARMS will allow evaluation of trends in the susceptibility of the organisms causing disease to the drugs used to treat them. For more information on antimicrobial resistance issues or the NARMS program visit CVM's web site at **www.fda.gov/cvm**. To review the NARMS Annual Reports use the specific Internet addresses given in the section "Where Can I find NARMS Data?"

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